CLARKE et al Appl. No. 09/529,342 January 25, 2007

RECEIVED CENTRAL FAX CENTER

## AMENDMENTS TO THE CLAIMS:

JAN 2 5 2007

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-41 (Cancelled).

- 42. (Previously Presented) A method of detecting a cell type of interest present or potentially present in a sample comprising treating the sample with lipid vesicle particles which are targeted to a targeted cell type to be detected, said particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide, which is non-covalently attached thereto, which peptide, in response to a predetermined metabolic signal from the targeted cell, if present in the sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles, said particles further incorporating a species which is activated on said modulation of permeability, and monitoring directly or indirectly for the species.
- 43. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide comprises an integral protein of the lipid layer.
- 44. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide spans the lipid layer.

- (Previously Presented) The method according to claim 42, wherein the cytolytic 45. peptide is non-covalently attached to an outer lipid layer.
- (Previously Presented) The method according to claim 42, wherein the particles 46. comprise a binding agent capable of binding a particle to the cell type of interest when the particle is targeted thereto.
- (Previously Presented) The method according to claim 46, wherein the binding 47. agent is an antibody for binding to an antigen on the cell type of interest.
- (Previously Presented) The method according to claim 42, wherein a portion of 48. said particles have a first binding moiety and a further portion have a second binding moiety which is capable of binding with said first binding moiety whereby said particles are, or are capable of being, aggregated together.
- (Previously Presented) The method according to claim 48, wherein a collection of 49. particles are aggregated around a cell to be detected.
- (Previously Presented) The method according to claim 48, wherein the first binding 50. moiety on some particles is avidin or a derivative thereof, and the second binding moiety on other particles is biotin or a derivative thereof.

CLARKE et al Appl. No. 09/529,342 January 25, 2007

- 51. (Previously Presented) The method according to claim 42, wherein the cytolytic peptide is selected from the group consisting of GALA, Helical erythrocyte lysing peptide (HELP), KALA, and LAGA.
- 52. (Previously Presented) The method according to claim 42, wherein the cytolytic peptide is N, Myristic-GALA.
- 53. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide is selected from the group consisting of Amphotericin B, Alamethicin, Gramicidin, Melittin, Nigericin, P25, Polymixin B, Valinomycin, and Vibriolsin.
- 54. (Previously Presented) The method according to claim 42, wherein the species is a dye.
- 55. (Previously Presented) The method according to claim 42, wherein the species is an enzyme.
- 56. (Previously Presented) The method according to claim 55, wherein the enzyme is alkaline phosphatase, β-Galactosidase or asparaginase, or glucose oxidase.
- 57. (Previously Presented) The method according to claim 42, wherein the species is a co-factor or substrate for an enzyme.

- (Previously Presented) The method according to claim 42, wherein the cells to be 58. detected are pathogenic cells.
- (Previously Presented) The method according to claim 58 for analysing foodstuff 59. for the presence of pathogenic cells.
- (Previously Presented) The method according to claim 58 for analysing water 60. samples for the presence of pathogenic cells.
- (Previously Presented) The method according to claim 58 for detecting the 61. presence of pathogenic cells in a human or animal body.
- (Withdrawn) The method according to claim 42, wherein the metabolic signal 62. comprises a change in ion concentration.
- (Withdrawn) The method according to claim 62, wherein the ion is H<sup>+</sup>, Na<sup>+</sup>, Cl<sup>-</sup>, 63. HCO<sup>-</sup>, or K<sup>+</sup>.
- (Currently Amended) The method according to claim 42, wherein the metabolic 64. signal comprises a change in pH A method of detecting a cell type of interest present or potentially present in a sample comprising treating the sample with lipid vesicle particles which are targeted to a targeted cell type to be detected, said particles having at least one layer of

enveloping lipids and incorporating a cytolytic peptide, which is non-covalently attached thereto, which peptide, in response to a predetermined metabolic signal, which metabolic signal comprises a change in pH, from the targeted cell, if present in the sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles, said particles further incorporating a species which is activated on said modulation of permeability, and monitoring directly or indirectly for the species.

- 65. (Previously Presented) The method according to claim 42, wherein the metabolic signal comprises a change in pH, wherein the pH is above 6.
- 66. (Previously Presented) The method according to claim 42, wherein the metabolic signal comprises a change in pH, wherein the pH is above 7.
- 67. (Withdrawn) The method according to claim 42, wherein the metabolic signal comprises a change in gas concentration.
- 68. (Withdrawn) The method according to claim 42, wherein the metabolic signal comprises a change in carbon dioxide concentration.